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Synthesis of new alkoxy substituted 4-piperidinobenzylidene malononitrile (PDCST) nonlinear optical chromophores

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Abstract

The new alkoxy-substituted 4-piperidinobenzylidene malononitrile (PDCST) nonlinear optical chromophores were synthesized for investigation into substitutional effect on electrooptic properties and response time. The concise four-step procedure afforded PDCST skeleton with various alkoxy-substituted groups such as methoxy, ethoxy and isobutoxy. Structures were confirmed by H, C-NMR and EI-MS spectroscopic analysis.

Keywords. Nonlinear optical chromophores, 4-piperidinobenzylidene malononitrile (PDCST), bromination; formylation; Buchwald-Hartwing, Knoevenagel condensation.

1. INTRODUCTION

During the past decades, organic photorefractive (PR) materials have received considerable attention because of their potential application in communication, data storage and image processing devices [1-5]. To exhibit photorefractive property, PR materials have to possess both photoconductivity and optical nonlinearity simultaneously so that spatially oscillating space-charge field is formed under the illumination of non-uniform light generated by the interference of two coherent laser beams via an electro-optic effect. One of the categories of this material is photoconductive polymers doped with second order nonlinear optical (NLO) chromophores. The relationship between structure and NLO property of chromophores has been investigated, along with synthesis of new NLO chromophores and their characterization. The alkoxy chains attached to NLO chromophores are expected to provide free volume to each chromophore, which will result in the fast orientation behavior under applied electric field [6-9]. Continuing our work on synthesis and application of new PR materials [10-14], we report herein the synthesis of methoxy, ethoxy and isobutoxy substituted 4-piperidino-benzylidene-malononitrle (PDCST) derivatives for investigation into substitutional effect on electro-optic properties and response time.

2. EXPERIMENTAL

2.1. Materials and instruments

All reagents were purchased from Aldrich Chem. Co. Products were purified by chromatography on silica gel 60 (Merck). Melting point of products was measured on Electrothermal 9100, ^{1}H, ^{13}C-MNR; spectra were recorded on Varian Mecury 400MHz NMR spectrometer using $CDCl_3$ as solvent. EI-MS was measured on JMS-700 (Jeol, Japan). All the reactions were carried out under nitrogen or argon atmosphere.

2.2. General synthetic methods

Synthesis of 1,4-dibromo-2,5-dialkoxybenzene (2a, 2b, 2c)

To a solution of **1**(**a-c**) (50 mmol) dissolved in AcOH (150 ml), $ZnCl_2$ (15 g, 110 mmol) was added at once and the mixture was stirred until complete dissolution. Under rigorous exclusion of light, Br_2 (7 ml, ~130 mmol) in AcOH (10 ml) was added dropwise into the above solution for over 30 minutes. The reaction mixture was stirred at room

temperature (rt) for 5 hrs, then quenched with dilute aqueous NaOH solution. The white precipitate was filtered, washed with water and cooled MeOH (0 ^oC). The MeOH filtrate was concentrated to appearance of white precipitate which was filterred, washed to get 2nd crop. The combined crude products were recrystallized from mixture of $EtOH/CH_2Cl_2$ (4/1, v/v) to give crystals of **2a** in 75 % yield, **2b** in 68 % yield, **2c** in 57 % yield.

Compound **2a**: 1,4-dibromo-2,5-dimethoxybenzene; mp 145 ^oC; ^{1}H-NMR δ 7.12 (2H, s, H-3, H-6 of ArH), 3.90 (6H, s, 2 × OC$\underline{H_3}$). Compound **2b**: 1,4-dibromo-2,5-diethoxybenzene; mp 132^{o}C; ^{1}H-NMR δ 7.02 (2H, s, H-3, H-6 of ArH), 4.02 (4H, q, 2 × OC$\underline{H_2}$-), 1.45 (6H, t, 2 × C$\underline{H_3}$). Compound **2c**: 1,4-Dibromo-2,5-diisobutoxybenzene; mp 54^{o}C; ^{1}H-NMR δ 7.06 (2H, s, H-3, H-6 of ArH), 3.72 (4H, d, 2 × OC$\underline{H_2}$), 2.13 (2H, septet, 2 × C$\underline{H}$ $(CH_3)_2$), 1.07 (12H, d, 4 × C$\underline{H_3}$).

Synthesis of 1'-(4-bromo-2,5-dialkoxy-phenyl)piperidine (3a, 3b, 3c)

A solution of BINAP (0.3 g, 0.4 mmol) and $Pd_2(dba)_3$ (0.3 g, 0.3 mmol) in toluene (150 ml) was stirred at rt for 30 minutes and 1,4-dibromo-2,5-dialkoxybenzene (**2a-c**) (30 mmol) was added, then the mixture was stirred at rt for 30 minutes before NaO *t*-Bu (3.4 g, 35 mmol) was added. The reaction mixture was heated to 96-100 ^oC and piperidine (3.0 g, 35 mmol) was added dropwise for one hour, then the stirring was continued at 95-100 ^oC for 5 hrs. After that, the reaction mixture was cooled to rt, water (100 mL) was added and the mixture was extracted with diethyl ether for three times. The ethereal layers were combined and washed with water, dried over anhydrous $MgSO_4$ then evaporated in vacuo and the product was purified by column chromatography on silica gel using *n*-hexane/EtOAc (9/1) as eluent to afford pure compounds **3a** in 62 % yield, **3b** in 58 % yield, **3c** in 47 % yield.

Compound **3a**: 1'-(4-bromo-2,5-dimethoxyphenyl)piperidine; mp 79 ^oC; ^{1}H-NMR δ 6.96 and 6.56 (2H, 2×s, Ar-$\underline{H}$), 3.85 and 3.81 (6H, 2×s, OC$\underline{H_3}$), 2.97 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 1.75-1.58 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring). Compound **3b**: 1-(4-bromo-2,5-diethoxyphenyl)piperidine; mp 78 ^oC; ^{1}H-NMR δ 6.96 and 6.54 (2H, 2×s, Ar-$\underline{H}$), 4.04 and 3.99 (4H, 2×q, OC$\underline{H_2}$-), 2.98 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 1.73-1.57 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring), 1.43 (6H, t, 2×C$\underline{H_3}$). Compound **3c**: 1-(4-bromo-2,5-diisobutoxyphenyl)piperidine; mp 69 ^oC; ^{1}H-NMR δ 6.96 and 6.52 (2H, 2×s, Ar-$\underline{H}$), 3.73 and 3.69 (4H, 2×d, OC$\underline{H_2}$-), 2.98 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 2.12 (2H, 2×septet, C$\underline{H}$ $(CH_3)_2$), 1.62-1.58 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring), 1.08 and 1.06 (12H, 2×d, C$\underline{H_3}$).

Synthesis of 2,5-dialkoxy-4-piperidin-1-yl-benzaldehyde (4a, 4b, 4c)

A solution of 1.6 M *n*-BuLi/*n*-hexane (5 ml, 8 mmol) was added dropwise to a solution of 1-(4-bromo-2,5-dialkoxy-phenyl)piperidine **3(a-c)** (5 mmol) in dry THF (50 ml) at -78 ^oC, then the mixture was stirred continuously at this temperature for 1 hour and 1-formyl piperidine (2.83 g, 25 mmol) in anhydrous THF (10 ml) was slowly added for over 30 minutes. The reaction mixture was stirred at -78 ^oC for 30 minutes, then warmed to -5 ^oC and followed by quenching with saturate aqueous ammonium chloride solution. The resulted mixture was extracted with $CHCl_3$ (3×25 ml). The extract was washed with water, dried over anhydrous $MgSO_4$ then evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using *n*-hexane/EtOAc (8/2) as eluent to give **4a** (85 %), **4b** (78 %) and **4c** (72 %).

Compound **4a**: 2,5-dimethoxy-4-piperidin-1-yl-benzaldehyde; mp 92 ^oC; ^{1}H-NMR δ 10.25 (1H, s, H -C$\underline{H}$O), 7.22 and 6.39 (2H, 2×s, Ar-$\underline{H}$), 3.87 and 3.83 (6H, 2×s, OC$\underline{H_3}$), 3.10 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 1.77-1.60 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring). Compound **4b:** 2,5-diethoxy-4-piperidin-1-yl-benzaldehyde; mp 99 ^oC; ^{1}H-NMR δ 10.27 (1H, s, H -C$\underline{H}$O), 7.22 and 6.40 (2H, 2×s, Ar-*H*), 4.13 and 4.05 (4H, 2×q, OC$\underline{H_2}$-), 3.17 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 1.75-1.62 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring), 1.40 and 1.45 (6H, 2×t, C$\underline{H_3}$). Compound **4c**: 2,5-diisobutoxy-4-piperidin-1-yl-benzaldehyde; mp 89 ^oC; ^{1}H-NMR δ 10.31 (1H, s, H-C$\underline{H}$O), 7.22 and 6.47 (2H, 2×s, Ar-$\underline{H}$), 3.8 and 3.75 (4H, 2×d, OC$\underline{H_2}$-), 3.28 (4H, t, N-C$\underline{H_2}$ of piperidine ring), 2.15 (2H, 2×septet, C$\underline{H}$ $(CH_3)_2$), 1.75-1.65 (6H, m, -C$\underline{H_2}$-C$\underline{H_2}$-C$\underline{H_2}$- of piperidine ring), 1.05 (12H, d, C$\underline{H_3}$).

Synthesis of 2-(2,5-dialkoxy-4-piperidin-1-yl-benzaldehyde)-malononitrile (5a, 5b, 5c)

To a solution of 2,5-dialkoxy-4-piperidin-1-yl-benzaldehyde **4(a-c)** (6 mmol) in 30 ml of anhydrous EtOH, malononitrile (0.5 g, 8 mmol) was added at once and the mixture was stirred until turned into a homogeneous solution, few drops of piperidine were added. The reaction mixture was then stirred for 1 hour and refluxed for 30 minutes and cooled to room temperature. The orange precipitate was filtered, washed with a solution of $EtOH/H_2O$ (1/1, v/v) then recrystallized from CH_2Cl_2/EtOH (1/5, v/v). The recrystallization was

repeated 3 times to give pure compounds **5a** in 82 % yield, **5b** in 75 % yield, **5c** in 74 % yield.

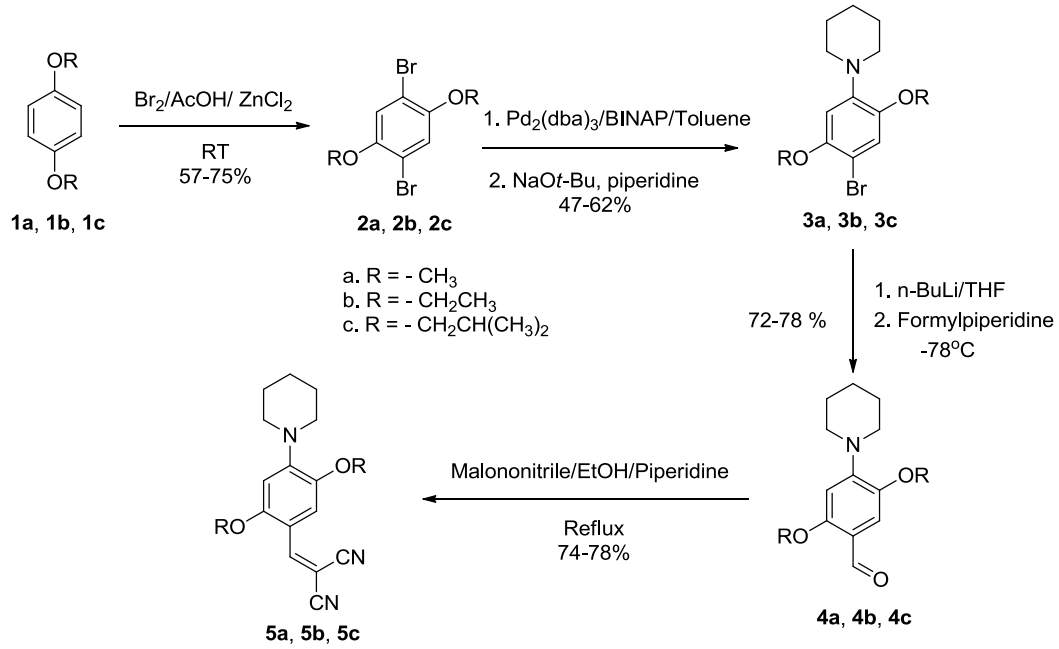
Compound **5a**: 2-(2,5-dimethoxy-4-piperidin-1-yl-benzylidine)-malononitrile; mp 176 ^{o}C; ^{1}H-NMR δ 8.12 (1H, s, –C*H*=C(CN)$_2$), 7.76 and 6.3 (2H, 2×s, Ar-*H*), 3.86 (6H, s, OC*H*$_3$), 3.3 (4H, t, N-C*H*$_2$ of piperidine ring), 1.75 - 1.65 (6H, m, -C*H*$_2$-C*H*$_2$-C*H*$_2$- of piperidine ring); ^{13}C-NMR δ 157.5, 152.7, 153.0, 146.4, 117.2, 116.3, 113.0, 110.5, 101.0, 73.4, 57.1, 57.0, 52.1, 26.98 25.2; EI-MS(m/z): 297[M]$^{+}$(100).

Compound **5b**: 2-(2,5-diethoxy-4-piperidin-1-yl-benzylidine)-malononitrile; mp 174 ^{o}C; ^{1}H-NMR δ 8.15 (1 H, s, –C*H*=C(CN)$_2$), 7.75 and 6.26 (2H, 2×s, Ar-*H*), 4.0-4.1 (4H, m, OC*H*$_2$-), 3.31 (4H, t, N-C*H*$_2$ of piperidine ring), 1.74 - 1.67 (6H, m, -C*H*$_2$-C*H*$_2$-C*H*$_2$- of piperidine), 1.46 and 1.45 (6H, 2×t, C*H*$_3$); ^{13}C-NMR δ 156.7, 152.4, 151.8, 145.3, 117.1, 116.1, 112.8, 111.0, 101.4, 72.5, 65.1, 65.1, 51.8, 26.5, 24.9, 15.41, 15.39; EI-MS (m/z): 325[M]$^{+}$(100).

Compound **5c**: 2-(2,5-diisobutoxy-4-piperidin-1-yl-benzylidine)-malononitrile; mp 98^{o}C; ^{1}H-NMR δ 8.09 (1H, s, –C*H*=C(CN)$_2$), 7.74 and 6.25 (2H, 2 × s, Ar-*H*), 3.78 and 3.74 (4H, 2×d, OC*H*$_2$-), 3.31 (4H, t, *N*-C*H*$_2$ of piperidine ring), 2.16 (2H, septet, C*H* (CH$_3$)$_2$), 1.75-1.67 (6H, m, -C*H*$_2$-C*H*$_2$-C*H*$_2$- of piperidine ring), 1.06 (12H, d, C*H*$_3$); ^{13}C-NMR δ 156.8, 152.2, 151.9, 145.6, 117.1, 116.1, 112.8, 110.1, 101.4, 76.1, 75.6, 72,6, 51.8, 29.1, 28.1, 24.9, 20.1, 20.0; EI-MS(m/z): 381[M]$^{+}$(100).

3. RESULTS AND DISCUSSION

Alkoxy substituted 4-piperidinobenzylidene malononitrile (PDCST) derivatives were synthesized in a four-step procedure as described in the scheme 1.



Scheme 1: Synthesis of alkoxy substituted 4-piperidinobenzylidene malononitrile (PDCST) chromophores

In step 1, the alkoxy arenes **1(a-c**) were brominated by reagent Br_2 in acetic acid using $ZnCl_2$ catalyst at room temperature and under rigorous exclusion of light to avoid substitution on the side chain. The alkoxy groups is ortho/para directing, so the bromination of **1(a-c**) afforded compounds 1,4-dibromo-2,5-dialkoxybenzene **2(a-c)**. In the step 2, Buchwald-Hartwig reaction was carried out between dibromo arenes **2(a-c**) and piperidine in toluene using $Pd_2(dba)_3$/BINAP catalyst and NaO*t*-Bu base to form C-N bond of obtained compounds **3(a-c**) in accepted yield (47-62 %). Next, the formylation of the aryl bromides **3(a-c**) was carried out using *n*-BuLi to metalate the aryl bromides **3(a-c**) then using *N*-formylpiperidine as transfer reagent to afford benzaldehyde compounds **4(a-c**) in high yield (72-78 %). Finally, Knoevenagel condensation of obtained aldehydes **4(a-c)** with malononitrile using catalytic piperidine gave crystalline products **5(a-c)** in high yield (74-78 %). The structures of the products were confirmed by ^{1}H, ^{13}C-NMR and EI-MS spectroscopic analysis. The ^{1}H, ^{13}C-NMR indicated signals of alkoxy groups such as the methoxy group (O*CH*$_3$) give signals at δ_H 3.8-3.9 (s) and δc 57.1-57.0; the ethoxy group give signals at δ_H 4.01-4.05 (q) and δc 65.1-65.1 of 2×O*CH*$_2$-), δ_H 1.40-1.45 (t) and δc 15.41, 15.39 of (2×*CH*$_3$); the isobutoxy groups give signals at δ_H 3.69-3.78 (d) and δc 75.6- 72.6 of (2×OCH$_2$-), δ_H 2.12-2.16 (septet) and δc 29.1, 28.1 of 2×C*H* (CH$_3$)$_2$), δ_H 1.05-

1.07 (m) and δc 20.1-20.0 of (4×$\underline{CH_3}$). The signals of piperizine ring at δ_H 2.97-3.7 (t) and δc 52.1-51.9 of 2×N-$\underline{CH_2}$; δ_H 1.57-1.75 (m) and δc 26.9-20.1 of (-$C\underline{H_2}$-$C\underline{H_2}$-$C\underline{H_2}$-). The signals of aromatic aldehyde group (Ar$\underline{CH}O$) at δ_H 10.25 (**4a**), δ_H 10.27 (**4b**), δ_H 10.31 (**4c**). The signals of the malononitrile moiety were indicated at δc 117.2, 116.3 (2×$\underline{C}$N), 73.4 (=$\underline{C}(CN)_2$) of **5a**; δc 117.1, 116.1 (2×$\underline{C}$N), 72.6 (=$\underline{C}(CN)_2$) of **5b**; δc 117.1, 116.1 (2×$\underline{C}$N), 76.1 (=$\underline{C}(CN)_2$) of **5c**.

4. CONCLUSION

We have repoted the synthesis of three new alkoxy-substituted 4-piperidinobenzylidene malononitrile (PDCST) nonlinear optical chromophores **5(a-c)** which will be used for further study on their non-linear electro-optic property which will be reported in due course.

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